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ORIGINAL ARTICLE

Causes and Prognosis of Unilateral and Bilateral Optic Disc Swelling

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ABSTRACT

The authors reviewed 93 consecutive cases with optic disc swelling (ODS) to compare clinical manifestations and prognosis among the causes. Among unilateral ODS patients ≥50 years old and without pain, anterior ischaemic optic neuropathy accounted for 87.5%. Furthermore, papilloedema (PE) presented unilateral ODS with an atrophic or hypoplastic disc in the opposite eye. Despite no differences for age and initial visual acuity between PE and pseudopapilloedema, the two main causes of bilateral ODS, some PE patients showed poor visual prognosis. Understanding differences in frequencies and clinical features of ODS related to cause and age group can help to accurately determine cause and predict outcome.

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Introduction

Optic disc swelling (ODS) is a characteristic presentation of various diseases, such as intrinsic ocular disease, as well as intracranial lesions and systemic diseases.[1,2] Although differential diagnosis of ODS includes various diseases, determination of cause is critical because of the many possible vision- or life-threatening diseases. Generally, most cases with bilateral ODS are considered to be caused by elevated intracranial pressure and should undergo a neuro-imaging examination or seek consultation at a department of neurology or neurosurgery. On the other hand, unilateral ODS is considered to be mainly caused by ocular conditions, such as anterior ischaemic optic neuropathy (AION) or optic neuritis (ON). Furthermore, differential diagnosis greatly differs between unilateral and bilateral ODS. An understanding of the frequencies of causes of ODS can help in deciding diagnostic examinations and predicting of prognosis. Jung et al. reported the causes of ODS in Korean population, and they compared non-arteritic AION and ON.[3] However, they could not investigate the causes of bilateral ODS in detail, because there were small number of cases in that study. In this study, we focused on the frequencies of both unilateral and bilateral ODS and also investigated differences in clinical features and prognosis.

Materials and methods

The current study was approved by the institutional review board (IRB) of Kyoto University Graduate School of Medicine, and all study conduct adhered to the tenets of the Declaration of Helsinki. According to our IRB guidelines, it was not mandatory to obtain informed consent from patients before retrospectively reviewing their medical records.

We retrospectively reviewed the clinical records of 93 consecutive patients with unilateral or bilateral ODS at the Neuro-ophthalmology Clinic of Kyoto University Hospital between April 2007 and March 2012.

Fundus examinations were performed and photographs obtained to determine the existence of ODS by neuro-ophthalmologists. For mild ODS or cases that were vague in fundus findings, we additionally performed optical coherence tomography and evaluated the thickness of the retinal nerve fibre layer (RNFL). Diagnosis of each disease was determined by the following criteria. ON was defined by the criteria of the Optic Neuritis Treatment Trial (ONTT) and non-arteritic AION

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(NA-AION) by the criteria of the Ischemic Optic Neuropathy Decompression Trial (IONDT).[4,5] Arteritic AION (A-AION) was diagnosed when patients presented typical clinical symptoms with erythrocyte sedimentation elevated to a level greater than the value obtained by dividing patient age by 2 in males and patient age plus 10 by 2 in females.[6] Papilloedema (PE) was diagnosed based on the presence of elevated intracranial pressure. Patients previously diagnosed with an intracranial disease and referred from a neurosurgery department with a putative diagnosis of papilloedema were excluded because they did not fulfil the differential diagnosis of ODS in ophthalmology findings. Diabetes mellitus papillopathy was diagnosed based on the existence of diabetes mellitus after excluding other possible diseases. Compressive optic neuropathy was confirmed by neuro-imaging findings. Pseudopapilloedema (PPE) was defined as an anomalous congenital elevation of the optic disc, known as a hypoplastic disc, a small cupping disc ratio, or the existence of optic disc drusen detected by ultrasound scanning, computed tomography, or autofluorescein imaging.[6] Other criteria for PPE were retinal vessels of normal calibre, spontaneous venous pulsations present, and no retinal or disc haemorrhage, as noted in a previous report.[7] Some cases with possible PE underwent neuro-imaging and lumbar puncture procedures to exclude PE. In all PPE cases, we confirmed that appearance was unchanged at the 6-month follow-up examination. Other diseases were diagnosed by characteristic clinical features and findings. The cases of ODS with uveitis were excluded from this study.

We investigated clinical features, age, sex, existence of ocular pain or headache, and change in visual acuity from the initial to final examination in patients who could be followed for more than 6 months or until complete recovery was confirmed. As for AION and ON, the two main causes of ODS, we compared the pattern of visual field defect, disc appearance of the unaffected eye, and existence of vasculopathic risk factors, such as diabetes mellitus, hypertension, hyperlipidaemia, cerebral infarction, and ischaemic heart disease.

Results

There were 21 (22.6%) cases with AION, 20 (21.5%) with ON, 18 (19.4%) with PE, 10 (10.8%) with PPE, and 24 with others (Table 1). The others included 6 patients with a disc tumour, 4 with infiltrative optic neuropathy, 4 with compressive optic neuropathy, and 3 with diabetes mellitus papillopathy (Table 2).

Comparisons of the four main causes of ODS are shown in Table 1. The AION group was relatively older than the other groups. Ocular pain or headache was common in both the ON and PE groups. Patients with AION and those with ON showed initial visual loss, whereas patients with PE or PPE tended to have no or mild visual disturbance at the first visit. Bilateral cases were relatively common in PE and PPE, although some of the AION and ON cases also presented bilateral ODS. On the other hand, some PE and PPE patients presented unilateral ODS.

Among the unilateral ODS cases, there were 18 (30.0%) with AION and 16 (26.7%) with ON. ON was common in patients <50 years old (41.9%), whereas AION was common in those ≥50 years old (51.7%) (Table 3). Furthermore, some unilateral ODS cases had PE (n = 2; 1 with optic atrophy in the opposite disc [Foster-Kennedy syndrome], 1 in whom the opposite disc was hypoplastic), compressive optic neuropathy, or infiltrative optic neuropathy.

Table 1. Comparisons of anterior ischaemic optic neuropathy, optic neuritis, papilloedema, pseudopapilloedema, and others.

Characteristic	AION (n = 21)	ON (n = 20)	PE (n = 18)	PPE (n = 10)	Others (n = 24)
Age (mean ± SD, years)	64.4 ± 11.5	38.9 ± 18.4	41.1 ± 17.8	38.7 ± 21.2	42.5 ± 19.4
Sex (Male/Female)	13/8	10/10	12/6	5/5	9/15
Bilateral (%)	3/21 (14%)	4/20 (20%)	16/18 (89%)	6/10 (60%)	4/24 (17%)
Pain (%)	4/21 (19%)	14/20 (70%)	12/18 (67%)	2/10 (20%)	5/24 (21%)
Initial VA (logMAR)	0.54 ± 0.79	0.77 ± 0.88	−0.06 ± 0.17	−0.09 ± 0.15	0.05 ± 0.24
Final VA (logMAR)	0.38 ± 0.76	0.11 ± 0.61	0.08 ± 0.64	−0.08 ± 0.17	0.28 ± 0.98

Note. AION = anterior ischaemic optic neuropathy; ON = optic neuritis; PE = papilloedema; PPE = pseudopapilloedema; VA = visual acuity.

Table 2. Causes of unilateral and bilateral optic disc swelling.

Cause	Unilateral optic disc swelling (n = 60)	Bilateral optic disc swelling (n = 33)
AION	18	3
A-AION	(6)	(1)
NA-AION	(12)	(2)
ON	16	4
PE	2	16
PPE	4	6
Small disc	(3)	(5)
Drusen	(1)	(1)
Others		
Disc tumour	6	—
Compressive optic neuropathy	4	—
Infiltrative optic neuropathy	3	1
Papillophlebitis	2	—
DM papillopathy	1	2
Neuroretinitis	1	—
Other	3	1

Note. ODS = optic disc swelling; AION = anterior ischaemic optic neuropathy; ON = optic neuritis; PE = papilloedema; PPE = pseudopapilloedema; AML = acute myeloid leukemia.

Table 3. Causes of unilateral and bilateral optic disc swelling in <50 years old or ≥50 years old.

	Unilateral optic disc swelling			Bilateral optic disc swelling		
Cause	Total	<50 years old	≥50 years old	Total	<50 years old	≥50 years old
ON	16	13	3	4	4	0
AION	18	3	15	3	0	3
PE	2	0	2	16	10	6
PPE	4	3	1	6	4	2
Others	20	12	8	4	1	3
Total	60	31	29	33	19	14

Note. AION = anterior ischaemic optic neuropathy; ON = optic neuritis; PE = papilloedema; PPE = pseudopapilloedema.

In a comparison of the differences between AION and ON, the two major causes of unilateral ODS, mean onset age in the AION cases was significantly older (64.4 ± 12.1 vs. 38.9 ± 18.4 years, $p < 0.001$) (Table 4). Complaints of ocular pain or headache were more common in ON than AION cases (70% vs. 19%, $p = 0.002$) (Table 4). In patients with unilateral ODS ≥50 years old and without pain (n = 16), AION accounted for 14 (87.5%). There was no significant difference between AION and ON in regard to initial visual acuity (0.54 ± 0.79 vs. 0.77 ± 0.88), although improvement in visual acuity was significantly greater in ON than in AION (−0.60 ± 0.83 vs. −0.13 ± 0.43, $p = 0.015$). The existence of vasculopathic risk factors, such as diabetes mellitus, hypertension, and hyperlipidaemia, was more

Table 4. Comparisons between anterior ischaemic optic neuropathy and optic neuritis.

Characteristic	AION (21 patients, 24 eyes)	ON (20 patients, 23 eyes)	p-value
Age (mean ± SD, years)	64.4 ± 11.5	38.9 ± 18.4	<0.001*
Symptom duration (days)	12.4 ± 8.9	13.1 ± 13.9	0.887*
Ocular pain or headache	4/21 (19%)	14/20 (70%)	0.002†
Risk factors for vasculopathic disease	8/14 (57%)	3/20 (15%)	0.023†
Visual field defect (eyes)	Lower altitudinal 10/24 (42%) Upper altitudinal 4/24 (17%) Central scotoma 3/24 (13%) General 5/24 (21%) Non-specific 2/24 (8%)	Central scotoma 9/17 (53%) General 5/17 (29%) Non-specific 3/17 (18%)	—
Disc appearance of unaffected opposite eye	Crowded 11/11 (NA-AION) Normal 6/6 (A-AION)	Normal 14/16 Pale 1/16 Myopic 1/16	—

Note. AION = anterior ischaemic optic neuropathy; ON = optic neuritis.
*Unpaired t-test.
†Fisher's exact test.

common in AION patients (57% vs. 15%, p = 0.023). As for patterns of visual field defects, lower and upper altitudinal field defects were common in AION (58%), whereas central scotoma was a major pattern in ON (53%). Disc appearance in the unaffected opposite eye was a crowded disc in all unilateral NA-AION cases. On the other hand, nearly all unaffected eyes in the A-AION and ON patients showed a normal disc. There were 3 bilateral cases in AION and 4 in ON. All cases of bilateral ON were young patients ranging from 13 to 24 years old.

The causes of bilateral ODS are shown in Table 2. Various conditions were shown in differential diagnosis of bilateral ODS. When bilateral ODS was divided into two groups based on age (<50, ≥50 years old), PE was a common cause in both (Table 3). Also, PE accounted for 48.5% of all cases of bilateral ODS. In cases of bilateral ODS accompanied with pain (n = 19), 12 (63.2%) were caused by PE. Although the primary diseases related to PE were primarily brain mass lesions

(7 of 16 cases), other diseases such as idiopathic intracranial hypertension (4 cases) and cerebral venous sinus thrombosis (2 cases) could not be confirmed by only computed tomography (CT) or magnetic resonance imaging (MRI) findings. The chief complaint in cases of PE was visual disturbance in 9 patients, headache or ocular pain in 4, and diplopia in 3, whereas 2 patients had no symptoms. Two of these 16 patients eventually showed visual acuity < 0.1, and 3 died of a brain tumour during the follow-up period. PPE was the second-most common cause in bilateral ODS cases. There were no significant differences in regard to visual acuity or age at the initial visit between the two main causes. However, nearly all PE cases required treatment and some showed poor visual prognosis, whereas none of the PPE patients showed changes in visual function, because of the entry criteria.

Discussion

We report the causes of unilateral and bilateral ODS as well as their frequency and also compared clinical features among the main causes. The major conditions associated with unilateral ODS were AION and ON, which previous reports showed to have some differences in regard to clinical features.[8,9] We also noted various diseases involved in bilateral ODS. Although PE should be differentiated from PPE, because of great differences in their treatments and prognosis, there were some similarities in regard to age and visual acuity at the initial visit. One of the contrasting points was found to be subjective symptoms such as pain, although it is difficult to completely differentiate the two diseases.

Patients with ODS caused by conditions other than AION and ON presented only mild visual dysfunction at the first visit, although the conditions could be vision-threatening or even fatal during the clinical course in some cases. Therefore, some of these patients required specific treatments. In addition, even unilateral ODS cases, which are mainly caused by AION or ON, included some with intracranial mass lesions, infiltration by a haematologic tumour, and sarcoidosis. Notably, when the unaffected opposite disc in unilateral ODS shows optic atrophy or is hypoplastic, indicating an inadequate number of viable nerve fibres, PE is a reasonable differential diagnosis and a neuro-imaging examination should be performed.

Differentiation between AION and ON is critical, because improvement in visual function is quite dissimilar, despite similar impairments in initial visual acuity. To differentiate these diseases, some useful clinical features have been reported, including pattern of visual field defect, onset age, existence of vasculopathic risk factors, pain, and optic disc appearance of the unaffected opposite eye.[10–13] For example, when the analysed cases were limited to unilateral ODS in patients ≥50 years old and without pain, AION accounted for 14 of 16 cases (87.5%). Understanding of these clinical features helps to accurately diagnose these two diseases.

Jung et al. mainly reported the causes of unilateral ODS in the Korean population.[3] Our result indicating AION and ON as the two major causes of unilateral ODS was concurrent with their report. However, their study did not include cases of A-AION, and there were 8 eyes of 7 patients with A-AION and 16 eyes of 14 patients with NA-AION in our study. A-AION may not be a rare condition in Japan, and A-AION should be carefully differentiated, given its bilateral progression in the absence of proper treatment.

As expected, PE was the main cause in bilateral ODS, whereas the differential diagnoses varied widely. In fact, more than 50% of the bilateral ODS cases were caused by other than PE. Furthermore, more than one third of cases with PE were idiopathic intracranial hypertension (IIH) or cerebral venous sinus thrombosis, which are not detected by MRI or CT. In such cases, an additional neuro-imaging protocol such as MR venography (MRV) as well as lumbar puncture and laboratory tests are necessary in order to diagnose or not overlook a treatable condition.

PPE was the second-most common cause of bilateral ODS. Differentiation between PPE and PE is of great importance, because nearly all patients with PE require treatment, and some in the present study died or lost eyesight. Generally, PE has characteristic ophthalmoscopic features, including opacification of the RNFL, disc

hyperaemia, absent venous pulsations, splinter haemorrhage, and circumferential retinal folds.[14] In typical cases, differentiation is relatively easy, although some cases, especially mild PE, are difficult to differentiate from PPE. Additionally, as shown in this study, there are some similarities in clinical features, such as age and visual acuity at the initial visit. Although subjective symptoms such as pain are useful for differentiation to some extent, suspicious cases should be subjected to repeated detailed examinations.

In conclusion, there are characteristic clinical features related to the causes of unilateral and bilateral ODS. Knowledge of their differences and frequency is important to determine cause and predict prognosis.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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